REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of Claims

Claims 1, 3-5, 7-12, and 25-36 are currently pending in the application.

Objections to the Specification

The Examiner contends that mPEGMAL and mPEG2MALare trademarks. Applicant respectfully submits that the terms are used consistently with the manufacturer's use in their catalog (a copy of the relevant pages thereof are submitted herewith) where no trademarks are indicated or used.

Claim Rejections – 35 USC § 103

In point Claims 1, 3-5, 7-12 and 29-36 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Athwal et al. (WO01/94585) in view of Relton (WO97/45140) as is evidenced by the U.S. Pat. No. 6,171,586.

The Examiner alleges the buffer formulation taught by the ' 140 publication is suitable for stabilizing antibody formulation of Fab fragements, bispecific antibodies (p. 4, line 26, in particular) or modified antibodies as is evidenced in the '586 patent. The Examiner contends the formulation taught by the ' 140 publication in stabilizing an antibody and the claimed antibody formulation are identical. Thus, the antibody formulation being stable 25°C for at least twelve weeks is an expected property of the buffer formulation containing the antibody.

Applicant respectfully submits the Examiner has failed to establish a *prima facie* case of obviousness. The '140 publication neither teaches nor discloses the claimed formulations. The '140 publication neither teaches nor discloses an antibody formulation

of an antibody fragment modified by the covalently attachment of at least one nonproteinaceous polymer. The '140 publication is directed to a method of producing a concentrated antibody preparation. The only formulations taught in '140 (Example 4, p.19) require additional excipients (i.e. NaCl & polysorbate). There is no stability data in '140 to support the Examiner's conclusion that the formulation disclosed result in a stable formulation. While '140 may prophetically refer to Fab fragments there is no factual teaching that the formulations taught will in fact result in a stable formulation let alone a stable formulation of an antibody fragment modified by the covalently attachment of at least one nonproteinaceous polymer. Therefore, the Examiner's statement that "*the formulation taught by the ' 140 publication in stabilizing antibody and the claimed antibody formulation are identical*" (emphasis added) is factually not supported by the '140 publication.

The teachings of '586 fail to overcome the shortcomings of '140. The Examiner relies on '586 to allegedly teach stable formulations of modified antibodies. As the Examiner clearly admits the only modified antibodies taught by '586 are heteroconjugated antibodies such as biotin or avidin and thionitrobenzoate. '586 does not teach or disclose an antibody fragment modified by the covalently attachment of at least one nonproteinaceous polymer and there is no factual basis that the formulations of '586 result in stable formulations of an antibody fragment modified by the covalently attachment of at least one nonproteinaceous polymer. Furthermore, the '586 formulations require additional excipients (i.e. surfactant and polyol) and there is no room temperature stability data beyond one month. To the contrary the data of '586 shows and the patentee concludes that the formulations were only stable at 30°C for one month (Figure 19 and description of Figure 19 on column 4 lines 35-44). Therefore, the Examiner's statement that "*the antibody formulation being stable 25°C for at least twelve weeks is an expected property of the buffer formulation containing the antibody*" is factually inconsistent with the teachings of '586 and is contrary to the patentee's own conclusion.

While '585 may teach a PEG modified antibody fragment (CDP870) it does not teach or suggest the formulations of the present invention.

Consequently, one of skill in the art would not have been motivated to combine the teachings of the three publications believing to have a reasonable expectation of

sources in producing applicants' temperature stable antibody-nonproteinaceous polymer conjugate formulation as presently claimed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Contrary to the holding of the Examiner, applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness because the Examiner has failed to fulfill these requirements.

Where the prior art itself specifically teaches that the formulation of '586 results in only one month of stability at 30°C then there is no reasonable expectation of success for the claimed formulation have 12 week stability at 25°C. Where the prior art teaches that additional excipients are required to have a stable formulation then the present formulation lacking those excipients is not obvious. Finally there is no motivation to combine the references to achieve the presently claimed stable modified antibody formulation where the prior art teaches away. Therefore, applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness.

Applicants respectfully request the Examiner to reconsider the rejection of claims1, 3-5, 7-12 and 29-32 and withdraw the rejection under 35 U.S.C. §103 (a).

Double Patenting Rejections

Claims 1, 3-5, 7-12 and 29-36 are provisionally rejected under the judicially created doctrine of double patenting over pending claims 39-50 and 54-57 of copending Application No. 10/634,199.

In light of the current status of 10/634,199 the double patenting rejection is moot.

Claim Rejections – 35 USC § 112

The Examiner rejected Claims 1, 3-5, 7-12 and 29-36 under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner avers this is a New Matter rejection.

The Examiner asserts that the specification and the claims as originally filed purportedly do not provide a clear support for the phrase "wherein said antibody formulation is stable at 25 °C for at least 12 weeks" as in claim 1, "wherein said antibody formulation is stable at 40 °C for at least 12 weeks" as in claim 36.

As previously submitted applicant pointed out Example 2 provides support for the limitations in claims 1 and 36. Inexplicably, while the Examiner freely admits that Example 2 is directed to CDP870, which is a PEG modified antibody, Example 2 provides data that the exemplified formulations are stable at 25 °C for at least 12 weeks (Table 1) as in claim 1, and at 40 °C for at least 12 weeks (Table 1) as in claim 36, the Examiner contends the limitations constitutes new matter. It is respectfully submitted the limitation is fully supported as exemplified since it has been shown that the formulation is stable at the recited temperatures and for the recited length of time and therefore cannot constitute new matter. While only CDP870 was exemplified in Example 2 the results fully support the limitation of the broader claimed invention.

The Examiner contends that while the specification ([0027]) provides support for a methoxypoly(ethyleneglycol) polymer it does not disclose a particular number and specifically not "at least two methoxypoly(ethyleneglycol) polymer" as in claim 34

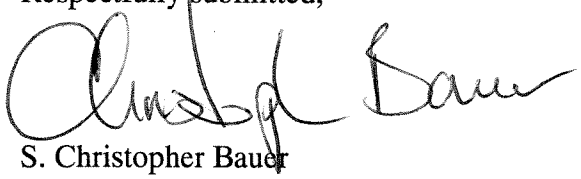
For further support for the limitation applicant directs the Examiner's attention to paragraphs [0028] and [0029] (pages 8 & 9) which shows the formula for CDP870, which clearly has two mPEGs and the description of the polymer moiety which describes it has having two mPEGs attached through a lysine linker. In addition applicant directs the Examiner to paragraph [0008] (page 3), in which the Examiner

had objected to the term "mPEG2MAL" as a being a trademark (as discussed above). The description clearly describes the polymer moiety has having two mPEGs linked through a lysine. It is respectfully submitted that "two methoxypoly(ethyleneglycol)s" is fully supported and therefore does not constitute new matter.

Conclusion

Applicants respectfully submit that all the grounds for rejection of the pending claims have now been overcome and that all the claims are now in condition for allowance. Therefore, swift passage of the application and claims to issue is respectfully requested. In the event that the Examiner wishes to discuss any aspect of this response for purposes of advancing the prosecution, please contact the undersigned representative at the telephone number provided below.

Respectfully submitted,



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